

Applicant: Robert J. Peach, et al.
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Please amend the subject application as follows.

In the Claims:

In compliance with the practice guidelines for making amendments under 37 C.F.R. § 1.121(c)(1), Applicants present all pending claims with status indicators. Please cancel claims 94, 97-103, 110-112, and 115 without prejudice, while reserving the right to prosecute such claims in related applications.

Please amend claims 67-80, 86, 95-96, 104-108, and 113-114 as follows.

--1 to 66. (CANCELED)

--67. (CURRENTLY AMENDED) A ~~soluble~~-CTLA4 mutant molecule which binds CD80 and/or CD86 comprising an extracellular domain of CTLA4 as shown in SEQ ID NO:8 ~~SEQ ID NO: 8~~ beginning with alanine at position 26 or methionine at position 27 and ending with aspartic acid at position 150, or a portion thereof, wherein in the extracellular domain or portion thereof an alanine at position 55 is substituted with a tyrosine, and a leucine at position 130 is substituted with a glutamic acid. --

--68. (CURRENTLY AMENDED) A ~~soluble~~-CTLA4 mutant molecule comprising:
(a) an amino acid sequence beginning with methionine at position 27 and ending with aspartic acid at position 150 of ~~SEQ ID NO: 4~~ SEQ ID NO:4,
or
(b) an amino acid sequence beginning with alanine at position 26 and ending with aspartic acid at position 150 of ~~SEQ ID NO: 4~~ SEQ ID NO:4. --

--69. (CURRENTLY AMENDED) A ~~soluble~~ CTLA4 mutant molecule comprising:

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- (a) an amino acid sequence beginning with methionine at position 27 and ending with aspartic acid at position 150 of ~~SEQ ID NO: 4~~ SEQ ID NO:4 or a portion thereof that binds CD80 and/or CD86, or
- (b) an amino acid sequence beginning with alanine at position 26 and ending with aspartic acid at position 150 of ~~SEQ ID NO: 4~~ SEQ ID NO:4 or a portion thereof that binds CD80 and/or CD86. --

--70. (CURRENTLY AMENDED) The ~~soluble~~ CTLA4 mutant molecule of claim 67, 68, or 69 further comprising an amino acid sequence which alters the solubility or affinity of the soluble CTLA4 mutant molecule. --

-- 71. (CURRENTLY AMENDED) The ~~soluble~~ CTLA4 mutant molecule of claim 70, wherein the amino acid sequence ~~amino acid sequence~~ which alters the solubility or affinity comprises an immunoglobulin. --

--72. (CURRENTLY AMENDED) The ~~soluble~~ CTLA4 mutant molecule of claim 71, wherein the ~~immunoglobulin~~ immunoglobulin is an ~~immunoglobulin~~ immunoglobulin constant region or portion thereof. --

--73. (CURRENTLY AMENDED) The ~~soluble~~ CTLA4 mutant molecule of claim 72, wherein the ~~immunoglobulin~~ immunoglobulin constant region or portion thereof is mutated to reduce effector function. --

--74. (CURRENTLY AMENDED) The ~~soluble~~ CTLA4 mutant molecule of claim 72 or 73, wherein the ~~immunoglobulin~~ immunoglobulin constant region comprises a hinge, CH2 and CH3 regions of an immunoglobulin molecule. --

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- 75. (CURRENTLY AMENDED) The ~~soluble~~-CTLA4 mutant molecule of claim 72, wherein the ~~immunoglobulin~~-immunoglobulin constant region or portion thereof is a human or monkey immunoglobulin constant region. --
- 76. (CURRENTLY AMENDED) A ~~soluble~~-CTLA4 mutant molecule comprising:
- (a) an amino acid sequence beginning with methionine at position 27 and ending with lysine at position 383 of ~~SEQ ID NO: 4~~-SEQ ID NO:4, or
 - (b) an amino acid sequence beginning with alanine at position 26 and ending with lysine at position 383 of ~~SEQ ID NO: 4~~-SEQ ID NO:4. --
- 77. (CURRENTLY AMENDED) A ~~soluble~~-CTLA4 mutant molecule consisting of:
- (a) an amino acid sequence beginning with methionine at position 27 and ending with lysine at position 383 of ~~SEQ ID NO: 4~~-SEQ ID NO:4, or
 - (b) an amino acid sequence beginning with alanine at position 26 and ending with lysine at position 383 of ~~SEQ ID NO: 4~~-SEQ ID NO:4. --
- 78. (CURRENTLY AMENDED) The ~~soluble~~-CTLA4 mutant molecule of claim 67, 68, 69, or 76 further comprising an amino acid sequence which permits secretion of the soluble CTLA4 mutant molecule. --
- 79. (CURRENTLY AMENDED) The ~~soluble~~-CTLA4 mutant molecule of claim 78, wherein the amino acid sequence which permits secretion comprises an oncostatin M signal peptide. --
- 80. (CURRENTLY AMENDED) A ~~soluble~~-CTLA4 mutant molecule comprising an amino acid sequence beginning with methionine at position 1 and ending with lysine at position 383 of ~~SEQ ID NO: 4~~-SEQ ID NO:4. --

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- 81. (WITHDRAWN) A nucleic acid molecule encoding the soluble CTLA4 mutant molecule of claim 67, 68, 69, 76, 77 or 80. --
- 82. (WITHDRAWN) The nucleic acid molecule of claim 81 comprising:
- (a) the nucleic acid molecule beginning with adenine at position 79 and ending with thymine at position 450 of SEQ ID NO:3, or
 - (b) the nucleic acid molecule beginning with guanine at position 76 and ending with thymine at position 450 of SEQ ID NO:3. --
- 83. (WITHDRAWN) The nucleic acid molecule of claim 81 comprising:
- (a) the nucleic acid molecule beginning with adenine at position 79 and ending with adenine at position 1149 of SEQ ID NO.: 3, or
 - (b) the nucleic acid molecule beginning with guanine at position 76 and ending with adenine at position 1149 of SEQ ID NO:3. --
- 84. (WITHDRAWN) The nucleic acid molecule of claim 81 comprising the nucleic acid molecule beginning with adenine at position 1 and ending with adenine at position 1149 of SEQ ID NO.: 3. --
- 85. (WITHDRAWN) A DNA molecule encoding a soluble CTLA4 mutant molecule, wherein the DNA molecule is deposited as ATCC No. PTA-2104. --
- 86. (CURRENTLY AMENDED) A ~~soluble~~ CTLA4 mutant molecule encoded by the nucleic acid molecule designated ATCC No. PTA-2104. --
- 87. (WITHDRAWN) A vector comprising the nucleic acid molecule of claim 81. --
- 88. (WITHDRAWN) A vector comprising the DNA molecule of claim 85. --

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- 89. (WITHDRAWN) A vector encoding a soluble CTLA4 mutant molecule and deposited with the ATCC as ATCC No. PTA-2104. --
- 90. (WITHDRAWN) A host cell having the vector of claim 87, 88, or 89. --
- 91. (WITHDRAWN) The host cell of claim 90 which is a bacterial or eukaryotic cell.
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- 92. (WITHDRAWN) The host cell of claim 91, wherein the eukaryotic cell is a COS cell or a Chinese Hamster Ovary (CHO) cell. --
- 93. (WITHDRAWN) A method for producing a soluble CTLA4 mutant molecule comprising growing the host cell of claim 90 so as to produce the soluble CTLA4 mutant molecule in the host cell, and recovering the molecule so produced. --
- 94. (CANCELLED)
- 95. (CURRENTLY AMENDED) A ~~soluble~~-CTLA4 mutant molecule comprising the entire extracellular domain of the soluble CTLA4 mutant molecule encoded by the nucleic acid molecule designated ATCC No. PTA-2104. --
- 96. (CURRENTLY AMENDED) A pharmaceutical composition comprising a ~~soluble~~-CTLA4 mutant molecule of claim 67, 68, 69, 76, 77, 94-86, or 95 and a pharmaceutically acceptable carrier. --
- 97 to 103. (CANCELLED)

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- 104. (CURRENTLY AMENDED) The CTLA4 mutant molecule of claims ~~99-71~~, wherein the ~~immunoglobulin moiety-immunoglobulin~~ comprises a hinge and any or all of the cysteine residues within the hinge are substituted with serine. --
- 105. (CURRENTLY AMENDED) The CTLA4 mutant molecule of claim 104, wherein a cysteines at position ~~+130-+156~~ is substituted with a serine, a cysteine at position ~~+136-+162~~ is substituted with a serine, and a cysteine at position ~~+139-+165~~ is substituted with a serine, as shown in ~~Figure 7~~ SEQ ID NO:4. --
- 106. (CURRENTLY AMENDED) The CTLA4 mutant molecule of claim ~~100-72~~, wherein the immunoglobulin constant region or portion thereof is mutated to include a cysteine at position ~~+130-+156~~ substituted with a serine, a cysteine at position ~~+136-+162~~ substituted with a serine, a cysteine at position ~~+139-+165~~ substituted with a serine, and a proline at position ~~+148-+174~~ substituted with serine, as shown in ~~Figure 7~~ SEQ ID NO:4. --
- 107. (CURRENTLY AMENDED) The CTLA4 mutant molecule of claim ~~99-71~~, wherein the ~~immunoglobulin moiety-immunoglobulin~~ comprises an amino acid sequence which begins with glutamic acid at position ~~+126-+152~~ and ends with lysine at position ~~+357-+383~~, as shown in ~~Figure 7~~ SEQ ID NO:4. --
- 108. (CURRENTLY AMENDED) The CTLA4 mutant molecule of claims ~~67, 68, or 69-97~~, further comprising a junction amino acid residue ~~which-and an immunoglobulin, where the junction amino acid residue is located between the~~ amino acid sequence which ends with aspartic acid at position ~~+124-+150~~ and the ~~immunoglobulin moiety-immunoglobulin~~. --
- 109. (PREVIOUSLY PRESENTED) The CTLA4 mutant molecule of claim 108, wherein the junction amino acid residue is glutamine. --

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--110 to 112. (CANCELLED)

--113. (CURRENTLY AMENDED) The CTLA4 mutant molecule of claims ~~97-67~~, 68, 69, 76 or 77, that has a slower dissociation rate from binding CD86 than wild type CTLA4. --

--114. (CURRENTY AMENDED) The CTLA4 mutant molecule of claims ~~97-67~~, 68, 69, 76, 77, 86, or 95, that is soluble. --

--115. (CANCELLED)